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INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 :
A01N 1/02, A61K 39/12, A61M 37/00, 5/14, B01D 15/04, 15/08, 61/00

A1

(11) International Publication Number: WO 95/16348

(43) International Publication Date: 22 June 1995 (22.06.95)

(21) International Application Number: PCT/US94/14227

(22) International Filing Date: 9 December 1994 (09.12.94)

(30) Priority Data:
08/168,438 17 December 1993 (17.12.93) US

(71) Applicant: BAXTER INTERNATIONAL INC. [US/US]; One Baxter Parkway. Deerfield, IL 60015 (US).

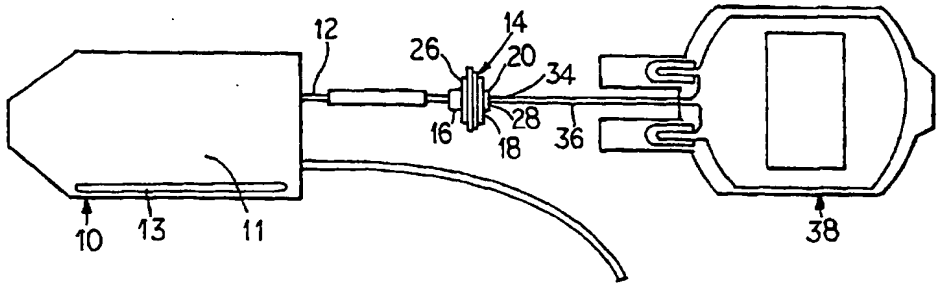
(72) Inventors: FOLEY, John, T.; 494 S. Navajo Trail, Wheeling, IL 60090 (US). CHAPMAN, John; 67 Kevin Avenue, Lake Villa, IL 60046 (US). WOLF, Ludwig, Jr.; 1417 Kirkwall, Inverness, IL 60010 (US).

(74) Agents: BARRETT, Joseph, B. et al.; One Baxter Parkway, Deerfield, IL 60015 (US).

(81) Designated States: AU, BR, CA, CN, JP, European patent (AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: METHOD AND APPARATUS FOR TREATING A BODY FLUID



(57) Abstract

A method for treating a body fluid to at least substantially inactivate viral contaminants that may be present therein comprising the steps of: providing a body fluid; adding to the body fluid a viral inactivating agent to create a resultant product; and passing the resultant product through a column including material having an affinity for the viral inactivating agent.

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SPECIFICATION

TITLE

METHOD AND APPARATUS FOR TREATING A BODY FLUID

BACKGROUND OF THE INVENTION

The present invention relates generally to the collection and therapeutic use of body fluids. More specifically, the present invention relates to methods and devices for attempting to substantially reduce or eliminate potential viral contaminants and other pathogens in body fluids, such as blood.

Of course, in a wide variety of therapies, such as transfusions and transplants, body fluids, especially blood components, such as red blood cells, platelets, plasma, and bone marrow, are infused from one or more individuals into a patient. Although such therapies provide treatments, many of which are life saving, and cannot otherwise be provided, due to the transmission of infectious diseases, there may be potential risks to such therapies.

For example, it is known that blood can carry infectious agents, such as hepatitis virus, human immune deficiency virus (an etiological agent for AIDS), cytomegalovirus, Epstein Barr virus, and herpes virus. Although screening methods exist to identify blood that may include such viruses, current screening methods do not assure that every blood unit that contains such a virus is identified.

For example, in this regard, one of the difficulties in testing blood components for viral contamination, such as HIV, is that many current diagnostic tests are based on an identification of antibodies. Therefore, a contaminated blood component will only exhibit a positive test if it includes antibodies for the virus, e.g., anti-

HIV. With respect to intracellular viral infections, an individual may not generate antibodies immediately upon infection. Rather, there is a window period that extends from the initial infection of the patient with a virus to the generation of antibodies. When an individual is in this window period, diagnostic tests that are based on antibodies will not identify the individual, or the blood unit, as being infected. But, even though the antibodies are not present, the blood unit can still transmit an infection.

With respect to HIV infection, it is believed that this window period can extend from approximately six weeks up to 48 months. During this time period, an individual who has been infected with HIV and accordingly, whose blood will transmit same, will register a negative antibody response. Currently used screening methods will not identify as contaminated a blood unit from an individual who is infected with HIV, but who has not generated anti-HIV.

In order to address the limitations of current diagnostic techniques and also to deal with the concern of transmission of viral contaminants and other pathogens to a patient receiving a transfusion, recent attention has focussed on the development of viral inactivating agents. It is envisioned that these viral inactivation agents would be added to the body fluid prior to the body fluid being administered to the patient.

For example, a number of photoactive agents that have antiviral action have been explored. These photoactive agents are generally agents that upon activation with light will inactivate or destroy pathogens, e.g., a virus that may be present. Such photoactive agents include: psoralens; porphyrins;

phthalocyanines; and dyes, such as methylene blue. See, for example, U.S. Patent Nos.: 4,748,120; 4,878,891; 5,120,649; and German Patent Application No. DE 39 30 510 A1 (Mohr).

Although such agents provide promise for the treatment of body fluids to eliminate the concern of viral contamination, there may be regulatory, as well as possible other concerns with respect to such agents. Of course, the resultant body fluid to which the anti-viral agent is added will be infused into a patient. Therefore, it is imperative that the agent does not create toxicity issues or other *in vivo* concerns.

With respect to photoactive agents, a still further issue is that upon activation of the agent and interaction of the agent with a virus, other products may be generated. For example, methylene blue is a photoactive agent that has been shown to have efficacy in inactivating viral contamination in plasma. Although methylene blue has been, through exhaustive testing, shown to have no toxicity concerns, upon photoactivation of methylene blue, photoproducts are generated. Specifically, Azure A and B are generated upon photoactivation of methylene blue. The *in vivo* effect of these products has not been as well studied as methylene blue in patients and therefore they raise regulatory issues and *in vivo* concerns.

There therefore is a need for an improved method and system for treating a body fluid to substantially reduce, if not eliminate, viral contaminants that may be present therein.

SUMMARY OF THE INVENTION

The present invention provides a method of treating a body fluid to substantially inactivate viral

contaminants that may be present therein. Pursuant to the method, to a body fluid is added a viral inactivation agent. The resultant product is then passed through a container, e.g., column including a material having an affinity for the viral inactivating agent. This allows the column to remove excess viral inactivating agent. Additionally, other products, e.g. photoproducts, that may be generated upon addition of the viral inactivation agent or any activation thereof are also eliminated. The body fluid can then be infused into a patient without regulatory or toxicity concerns.

To this end, in an embodiment, the present invention provides a method for treating a body fluid to at least substantially inactivate viral contaminants that may be present comprising the steps of: providing a body fluid; adding to the body fluid a viral inactivating agent to create a resultant product; and passing the resultant product through a column including material having an affinity for the viral inactivating agent.

In an embodiment, the material includes charcoal.

In an embodiment, the column is an ion exchange column.

In an embodiment, the material includes neural macroporous polymeric beads with a high surface area for absorbing organics from aqueous solutions.

In an embodiment, the viral inactivating agent is a light activated agent.

In an embodiment, the viral inactivating agent is chosen from the group consisting of: porphyrins; psoralens; phthalocyanines; and dyes.

The present invention also provides a method for treating a blood product comprising the steps of: providing a blood product; adding to the blood product

a light activated viral inactivating agent to create a resultant product; irradiating the resultant product with light of a sufficient wavelength to activate the viral inactivating agent to create a further product; passing the further product through a column having an affinity for the viral inactivating agent; and collecting a product that passes through the column.

In an embodiment, the blood product includes platelets and the viral inactivating agent is a psoralen.

In an embodiment, the blood product includes plasma and the viral inactivating agent includes methylene blue.

In an embodiment, the column also has an affinity for photoproducts generated by irradiating the resultant product.

The present invention also provides a method for providing a blood product to a patient comprising the steps of: collecting a blood product from a donor; adding to the blood product a light activated viral inactivation agent; irradiating the blood product and light activated viral inactivation agent with light of a sufficient wavelength to activate the viral inactivation agent to create a resultant product; passing the resultant product through a column having an affinity for the viral inactivation agent; collecting a resultant blood product that passes through the column; and administering the resultant blood product to a patient.

An advantage of the present invention is that it provides an improved method for treating a body fluid to at least substantially inactivate viral contaminants that may be therein.

Another advantage of the present invention is that it provides a method for inactivating or eliminating

pathogens from blood or its components before they are infused into a patient.

Furthermore, an advantage of the present invention is that it provides a system that allows viral inactivating agents to be added to a body fluid before the fluid is infused into a patient and eliminate toxicity or regulatory concerns.

Still further, an advantage of the present invention is that it provides a method for eliminating photoproducts from a system that adds a photoactive agent to a body fluid.

Moreover, an advantage of the present invention is that it prevents any post thaw photoactivation of excess photoactivated agents.

Another advantage of the present invention is that it allows normal plasma color for treated plasma.

Additional features and advantages of the present invention are described in, and will be apparent from, the detailed description of the presently preferred embodiments and from the drawings.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1 illustrates, schematically, an embodiment of the system of the present invention.

Figure 2 illustrates graphically results of Example No. 3 and specifically, the content of fibrinogen in reference plasma, post-thaw, pretreatment, post treatment, and post removal.

Figure 3 illustrates graphically results of Example No. 3 and specifically, the content of Factor V in reference plasma, post-thaw, pretreatment, post treatment, and post removal.

Figure 4 illustrates graphically results of Example No. 3 and specifically, the content of Factor VII in

reference plasma, post-thaw, pretreatment, post treatment, and post removal.

Figure 5 illustrates graphically results of Example No. 3 and specifically, the content of Factor VIII:C in reference plasma, post-thaw, pretreatment, post treatment, and post removal.

Figure 6 illustrates graphically results of Example No. 3 and specifically, the content of Factor IX in reference plasma, post-thaw, pretreatment, post treatment, and post removal.

Figure 7 illustrates graphically results of Example No. 3 and specifically, the content of Factor XI in reference plasma, post-thaw, pretreatment, post treatment, and post removal.

Figure 8 illustrates graphically results of Example No. 3 and specifically, the content of prothrombin in reference plasma, post-thaw, pretreatment, post treatment, and post removal.

Figure 9 illustrates graphically results of Example No. 3 and specifically, the content of activated partial thromoplastin time in reference plasma, post-thaw, pretreatment, post treatment, and post removal.

DETAILED DESCRIPTION

OF THE PRESENTLY PREFERRED EMBODIMENTS

The present invention provides a method and apparatus for use in treating a body fluid, such as blood, to reduce or eliminate viral contaminations that may be present therein. It is believed that the present invention can be used with a variety of viral inactivating agents. Such agents include, without limitation, photoinactivation agents, such as psoralens, porphyrins, dyes, such as methylene blue,

phthalocyanines, phenothiazines, hypericin, and other compounds that are activated by light.

As has been suggested in the art, a photoactive viral inactivating agent would be added to a body fluid, such as blood prior to the blood being infused into a patient. The resultant blood product including the photoactive agent then would be activated by light of a suitable wavelength. Of course, if desired, other viral inactivating agents that are not based on activation through light can be utilized in the present invention.

Pursuant to the present invention, as illustrated in Figure 1, a container 10 will be provided including, for example, a blood component 11. The blood component have added thereto a viral inactivation agent 13.

For example, it is known to collect whole blood in a blood pack. Typically, whole blood is then separated into its component parts. After the blood is separated into the respective components, using a system such as the Optipress® system marketed by affiliates of Baxter International, the blood component can be added to the container 10 including the viral inactivation agent. For example, methylene blue can be added to the plasma component. Of course, if desired, whole blood can be treated with a viral inactivation process. Likewise, if desired, a separate container is not required and the viral inactivation agent can be added to the container in whcih the component is stored.

The container 10 will include a fluid line 12 that will be coupled to a column 14. As used herein, column refers broadly to a chamber or device that includes material that will remove specific compounds or entities. Accordingly, column includes cartridges, containers, and other means for housing such material.

Pursuant to the present invention, the column 14 will include materials having an affinity for the viral inactivation agent and photoproducts generated thereby. The column will include an inlet 16 allowing product to flow into an interior 18 defined by the housing 20. In an embodiment, porous plates (not illustrated) are located at each end 26 and 28, respectively, of the interior 18 of the housing 20. The porous plates allow the body fluid to flow through an affinity matrix located therein. The resultant product then flows out of the cartridge 14 through the outlet 34.

In use, after the container containing the blood product and viral inactivation agent is activated by light of an appropriate wavelength, the resultant product flows through fluid line 12 and into the affinity column 14. The affinity column 14 will remove excess viral inactivation agents, as well as photoproducts. For example, with respect to methylene blue, excess methylene blue will be removed, as well as Azure A and B. The resultant blood product will then flow through fluid line 36 to a container 38. The blood can be stored in the container 38 and then infused into a patient.

To allow selective flow through the fluid line 12, breakable cannulas, as are known in the art, can be provided. Of course, other means for allowing selective flow through the fluid line 12 can be provided.

It should be noted that although in the illustrated embodiment the cartridge 14 is a separate and distinct component from the container 10, a unitary structure can be provided. In this regard, the column can be integral with the container or coupled thereto as an outlet port of the container.

The material used for the matrix in the affinity column 14 can comprise a variety of different materials. For example, charcoal, an ion exchange resin, or biobeads can be used. As used herein, the term "biobeads" refers to neural macroporous polymeric beads with a high surface area for adsorbing organics from aqueous solutions. Biobeads can vary in their hydrophilic and hydrophobic polarities. The range of believed useful properties of biobeads for the present invention is as follows: polarity (non-polar to intermediate polarity); Dipole Moment (0.1 to 3.0); bead size (30 to 2000 μm); average pore diameter (45 to 300 angstroms); bead surface area (150 to 1,600 sq. meters/gram dry bead). It has been found that biobeads available from Biorad Laboratories, 2000 Alfred Nobel Drive, Hercules, CA 94547 under the name Macro-Prep® t-butyl HIC function satisfactorily to remove methylene blue and methylene blue photoproducts Azure A and B.

By way of example, and not limitation, examples of the present invention will now be given:

EXAMPLE NO. 1

Removal studies were performed on 4'-aminomethyl-4,5',8-trimethyl psoralen (AMT). Specifically, three studies were performed, two using activated charcoal columns and one using an ion exchange column. The charcoal columns each consisted of 5.3 grams of activated charcoal obtained from a commercial water purification device. The ion exchange column consisted of less than 8.2 grams of Biorad AG 50W-X8 cation exchange resin.

One unit (80 mL) of plasmalyte platelets containing 40 ug/mL of AMT was passed through the first charcoal filter at a rate of about 30 mL/min. This column removed 86% of the AMT as measured by HPLC. Platelet loss going

through the column was 6%. Total protein was reduced by 33%. The platelet morphology score dropped from 355 to 315.

A second charcoal column was tested at a flow rate of about 5 mL/min. This column removed "100%" of the AMT as measured by HPLC. Platelet loss was 14%. Total protein increased by 14%. The platelet morphology score was unchanged by the column (200).

It is clear from these data that the activated charcoal can remove significant amounts of the AMT drug. The removal is inversely proportional to flow rate. The charcoal also appears to remove about one third of the plasma protein and 6-7% of the platelets. At the reduced flow rate (higher drug removal) the platelet morphology score dropped appreciably. We did not see any "fines" coming off the charcoal column.

The ion exchange column clearly removed significant amounts of AMT at low flow rate, but not as much as the charcoal. This column did not appear to remove any plasma protein and platelet loss was higher than with the charcoal. The platelets did not appear to be effected by the ion exchange resin.

EXAMPLE NO. 2

In this example, two more AMT removal studies were performed using biobeads, one with 5.5 grams of 100-200 mesh biobeads and the other with 7.5 grams of 20-50 mesh biobeads.

One unit (50-60 mL) of platelets (in lactated ringers) containing about 20 ug/mL of AMT was pumped through each column at a rate of 7 mL/min. Both columns removed all measurable AMT, but the 20-50 mesh column material yielded a "cleaner" HPLC output. The platelet loss for the 100-200 mesh column was 40% and for the 20-

50 mesh was 28%. Total protein was reduced by 13% in the 100-200 mesh column and by 32% in the 20-50 mesh. The platelet morphology for the 100-200 mesh column was unchanged passing through the column at 355, and for the 20-50 mesh column the morphology changed from 130 to 115. It should be noted that the unit of platelets used for the 20-50 mesh biobead column had low platelet counts, bad platelet morphology and low protein content. The columns did not appear to shed any "fines", nor did the beads swell.

The biobeads removed AMT as well as the activated charcoal tested in Example No. 1.

EXAMPLE NO. 3

The following method was performed on ten units of fresh frozen plasma, which had been thawed using an Instacool plasma thawer. An approximately 12 ml sample was collected from each unit as an untreated control sample and aliquoted into tubes for testing. The tubes were labeled with the protocol number, the sample letter and untreated. These units were stored frozen (-80°C±10°C) until analyzed.

TREATED SAMPLES

The following procedure was performed on ten units of fresh frozen plasma, which had been thawed using the Instacool plasma thawer. An approximately 12 ml untreated sample was removed from each unit, aliquoted and stored frozen (-80°C±10°C) until testing. Each unit was sterile connected and added to a container containing methylene blue. These units were labeled K-T. Each methylene blue treatment bag (PL732) was wrapped with aluminum foil and placed on a rotator (Scientific Products Multipurpose rotator Model 151) at room temperature and mix end-over-end at 40-60 rpm for 60

minutes. After mixing, the units were kept in aluminum foil and at room temperature prior to irradiation.

An approximately 16 ml pretreatment sample was removed from each unit and divided into a 4 ml aliquot for methylene blue testing. Prior to irradiation of the plasma units, the light output delivered by the irradiation box was measured. The light output was recorded. The methylene blue plasma mixture was irradiated with the LED light source. The LED light source was placed on top of a horizontal rotator at a speed of 60 rpm. All units were irradiated with red light for 8 J/cm^2 exposure. The start and stop times were noted.

An approximately 16 ml post treatment sample was removed from each unit and divided into a 4 ml aliquot for methylene blue testing. The remaining plasma in each plasma unit was passed through a methylene blue removal cartridge in the removal set of Figure 1 with a plasma expressor. The removal cartridge included biobeads obtained from Biorad Laboratories and sold under the name Macro-Prep® t-butyl HIC. An approximately 16 ml post removal sample was aseptically removed from each unit and divided into a 4 ml aliquot for methylene blue testing.

The following data was generated. Figures 2-9 graphically illustrate the data.

Methylene Blue (MB) (ug/ml)

		1uM=.374 ug/ml			
Test	Sample	untreated	pretreatment	post treatment	post removal
MB	K	NT	0.308	0.39	NRQ
MB	L	NT	0.316	0.365	NRQ
MB	M	NT	0.409	0.363	NRQ
MB	N	NT	0.368	0.329	NRQ
MB	O	NT	0.419	0.353	NRQ
MB	P	NT	0.401	0.348	NRQ
MB	Q	NT	0.422	0.306	NRQ
MB	R	NT	0.426	0.409	NRQ
MB	S	NT	0.43	0.344	NRQ
MB	T	NT	0.292	0.384	NRQ

*NRQ = No recoverable quantity

Prothrombin Time

Test	Sample	untreated	pretreatment	post treatment	post removal
PT	K	12	12	12.2	13.8
PT	L	11.9	11.8	12.4	11.9
PT	M	12.2	12.5	13.7	13.7
PT	N	11.5	11.5	11.8	11.4
PT	O	12.2	12.1	15.1	12.1
PT	P	13.6	12.5	13.4	12.5
PT	Q	11.7	12.1	13.8	12.1
PT	R	11.6	13.2	15.8	13.7
PT	S	11.8	12.1	13.8	13.2
PT	T	11.7	14.2	13.1	11.8
	AVG	12.02	12.4	13.51	12.62
	SD	0.603	0.782	1.249	0.900

Activated Partial Thromboplastin Time

Test	Sample	untreated	pretreatment	post treatment	post removal
APTT	K	37.1	34.2	35.9	39
APTT	L	26	26.6	26.9	27.3
APTT	M	28.6	30.4	35.7	28.4
APTT	N	31.7	31.1	32.3	29.7
APTT	O	31.2	32.5	38.9	31.3
APTT	P	38.9	31.8	36.3	33.6
APTT	Q	29.4	30.4	35.9	32.2
APTT	R	29.9	34.1	45.3	36.1
APTT	S	29.6	30.7	31.7	39.5
APTT	T	31.9	41.2	31.1	31.8
	AVG	31.43	32.3	35	32.89
	SD	3.882	3.801	4.990	4.185

Factor IX

Test	Sample	untreated	pretreatment	post treatment	post removal
Factor IX	K	117	92	94	96
Factor IX	L	100	87	76	87
Factor IX	M	61	59	60	54
Factor IX	N	79	75	81	69
Factor IX	O	68	75	72	65
Factor IX	P	70	63	45	51
Factor IX	Q	71	67	64	55
Factor IX	R	72	59	70	68
Factor IX	S	88	88	87	71
Factor IX	T	84	82	76	66
	AVG	81	74.7	72.5	68.2
	SD	16.964	12.338	13.986	14.227

Factor XI

Test	Sample	untreated	pretreatment	post treatment	post removal
Factor XI	K	132	118	122	80
Factor XI	L	121	105	96	76
Factor XI	M	118	94	67	44
Factor XI	N	109	104	96	78
Factor XI	O	132	128	126	68
Factor XI	P	77	69	65	43
Factor XI	Q	102	103	91	54
Factor XI	R	99	78	88	44
Factor XI	S	106	91	95	36
Factor XI	T	87	78	75	39
	AVG	108.3	96.8	92.1	56.2
	SD	18.087	18.564	20.431	17.492

Factor VII

Test	Sample	untreated	pretreatment	post treatment	post removal
Factor VII	K	103	95	92	104
Factor VII	L	129	119	119	116
Factor VII	M	63	57	57	61
Factor VII	N	87	84	82	93
Factor VII	O	89	85	89	90
Factor VII	P	59	63	50	60
Factor VII	Q	86	70	72	80
Factor VII	R	63	55	55	61
Factor VII	S	74	66	64	99
Factor VII	T	92	90	87	95
	AVG	84.5	78.4	76.7	85.9
	SD	21.324	20.001	21.250	19.723

Factor VIII:C

Test	Sample	untreated	pretreatment	post treatment	post removal
Factor VIII:C	K	47	41	41	44
Factor VIII:C	L	89	88	83	87
Factor VIII:C	M	93	81	81	71
Factor VIII:C	N	56	51	46	46
Factor VIII:C	O	104	101	88	85
Factor VIII:C	P	46	36	39	36
Factor VIII:C	Q	76	70	54	54
Factor VIII:C	R	53	43	46	44
Factor VIII:C	S	63	55	56	54
Factor VIII:C	T	92	75	62	66
	AVG	71.9	64.1	59.6	58.7
	SD	21.522	22.098	18.265	17.795

Fibrinogen

Test	Sample	untreated	pretreatment	post treatment	post removal
Fibrinogen	K	341	290	276	281
Fibrinogen	L	308	285	261	248
Fibrinogen	M	250	235	204	185
Fibrinogen	N	377	345	318	329
Fibrinogen	O	285	273	248	252
Fibrinogen	P	200	189	149	137
Fibrinogen	Q	308	284	212	214
Fibrinogen	R	273	248	223	235
Fibrinogen	S	241	244	196	191
Fibrinogen	T	299	266	257	255
	AVG	288.2	265.9	234.4	232.7
	SD	50.861	41.162	47.664	53.994

Factor V

Test	Sample	untreated	pretreatment	post treatment	post removal
Factor V	K	69	65	58	53
Factor V	L	84	80	74	77
Factor V	M	77	73	69	62
Factor V	N	84	79	74	71
Factor V	O	63	58	60	54
Factor V	P	74	67	62	53
Factor V	Q	71	63	52	49
Factor V	R	77	58	65	63
Factor V	S	73	62	59	60
Factor V	T	53	47	48	43
	AVG	72.5	65.2	62.1	58.5
	SD	9.384	10.130	8.634	10.244

CONTROL SAMPLES

Sample	Fibrinogen	Factor V	Factor VII
Reference	200-400	50-150%	65-135%
range	mg/dl		
A untreated	281	82	95
B untreated	249	114	144
C untreated	202	79	103
D untreated	302	62	76
E untreated	399	87	71
F untreated	233	96	82
G untreated	279	93	87
H untreated	263	58	113
I untreated	299	60	80
J untreated	240	111	98
AVG	274.7	84.2	94.9
SD	53.614	20.077	21.584

Sample	Factor VIII:C	Factor IX	Factor XI
Reference	50-150%	60-140%	65-135%
range			
A untreated	69	83	101
B untreated	83	115	107
C untreated	31	86	118
D untreated	62	79	101
E untreated	55	90	118
F untreated	96	97	80
G untreated	62	118	142
H untreated	99	85	130
I untreated	150	94	97

J untreated	83	98	103
AVG	79	94.5	109.7
SD	32.180	13.109	17.764

Sample	Prothrombin	APTT
	Time (sec)	(sec)
Reference		
range		
A untreated	12.3	30.7
B untreated	11.6	30.8
C untreated	12	31.5
D untreated	12.1	31
E untreated	11.7	28.4
F untreated	12.4	27.1
G untreated	11.7	25.1
H untreated	12.5	28
I untreated	12.9	28.2
J untreated	11.5	26.5
AVG	12.07	28.7
SD	0.455	2.179

After flowing through the cartridge less than 4 nanograms/ml of methylene blue and photoproducts were present in the blood. It should be noted that prior to removal, the blood unit contained 400 nanograms/ml methylene blue. By way of example for a 70 Kg man receiving 2 liters of methylene blue treated fresh frozen plasma he would receive, after removal pursuant to the present invention, 114 ng/Kg of methylene blue. This amounts to 1/44,000 that of normal intravenous clinical

dose. This reduced level effectively eliminates any toxicity concerns.

As illustrated in Figures 2-9, except for with respect to Factor XI, the removal step does not remove components from the plasma. Figures 2-9 illustrate, graphically content of specific components in: reference plasma; post-thaw; pretreatment; post treatment; and post removal. Specifically, Figures 2-9 graphically illustrate, content of: Fibrinogen; Factor V; Factor VII; Factor VII:C; Factor IX; Factor XI; prothrombin; and activated partial thromboplastin time, respectively. As illustrated, the method of the present invention can be used without destroying the therapeutic benefits of the blood to be transfused.

It should be understood that various changes and modifications to the presently preferred embodiments described herein will be apparent to those skilled in the art. Such changes and modifications can be made without departing from the spirit and scope of the present invention and without diminishing its attendant advantages. It is therefore intended that such changes and modifications be covered by the appended claims.

WE CLAIM:

1. A method for treating a body fluid to at least substantially inactivate viral contaminants that may be present therein comprising the steps of:

providing a body fluid;

adding to the body fluid a viral inactivating agent to create a resultant product; and

passing the resultant product through a column including material having an affinity for the viral inactivating agent.

2. The method of Claim 1 wherein the material includes charcoal.

3. The method of Claim 1 wherein the column is an ion exchange column.

4. The method of Claim 1 wherein the material includes biobeads.

5. The method of Claim 1 wherein the viral inactivating agent is a light activated agent.

6. The material of Claim 1 wherein the viral inactivating agent is chosen from the group consisting of: porphyrins; psoralens; phthalocyanines; phenothiazines; hypericin; and dyes.

7. The method of Claim 1 wherein the body fluid is a blood product.

8. The method of Claim 1 wherein the material has an affinity for derivatives of the viral inactivating agent.

9. The method of Claim 4 wherein the biobeads have the following characteristics:

polarity- non-polar to intermediate polarity;

Dipole moment - 0.1 to 3.0;

bead size - 30 to 2000;

average pore diameter 45 to 300 angstroms; and

bead surface area 15 to 1600 sq. meters/gram dry bead.

10. A method for treating a blood product comprising the steps of:

providing a blood product;

adding to the blood product a photosensitizer;

irradiating the photosensitizer with light of a sufficient wavelength to activate the photosensitizer;

passing the blood product through a column having an affinity for the photosensitizer; and

collecting a blood product that passes through the column.

11. The method of Claim 10 wherein the column includes charcoal.

12. The method of Claim 10 wherein the column is an ion exchange column.

13. The method of Claim 10 wherein the column includes biobeads.

14. The method of Claim 10 wherein the photosensitizer is chosen from the group consisting of: porphyrins; psoralens; phthalocyanines; phenothiazines; hypericin; and dyes.

15. The method of Claim 10 wherein the blood product is administered to a patient.

16. The method of Claim 10 wherein the blood product includes platelets and the photosensitizer is a psoralen.

17. The method of Claim 10 wherein the blood product includes plasma and the photosensitizer is methylene blue.

18. The method of Claim 10 wherein the column also has an affinity for photoproducts generated by irradiating the photosensitizer.

19. The method of Claim 10 wherein the photosensitizer is added to the blood product in a container separate from the column.

20. The method of Claim 10 wherein substantially all the blood product passes through the column.

21. A method for providing a blood product to a patient comprising the steps of:

collecting a blood product from a donor;

adding to the blood product a light activated viral inactivation agent;

irradiating the blood product and light activated viral inactivation agent with light of a sufficient wavelength to activate the viral inactivation agent to create a resultant product;

passing the resultant product through a column having an affinity for the viral inactivation agent;

collecting a resultant blood product that passes through the column; and

administering the resultant blood product to a patient.

22. The method of Claim 21 wherein the column includes charcoal.

23. The method of Claim 21 wherein the column is an ion exchange column.

24. The method of Claim 21 wherein the column includes biobeads.

25. The material of Claim 21 wherein the viral inactivating agent is chosen from the group consisting of: porphyrins; psoralens; phthalocyanines; phenothiazines; hypericin; and dyes.

26. The method of Claim 21 wherein the blood product includes platelets and the viral inactivating agent is a psoralen.

27. The method of Claim 21 wherein the blood product includes plasma and the viral inactivating agent includes methylene blue.

28. The method of Claim 21 wherein the column also has an affinity for photoproducts generated by irradiating the resultant product.

29. The method of Claim 21 wherein the viral inactivating agent is added to the blood product in a container separate from the column.

30. The method of Claim 21 wherein substantially all the blood product passes through the column.

FIG. 1

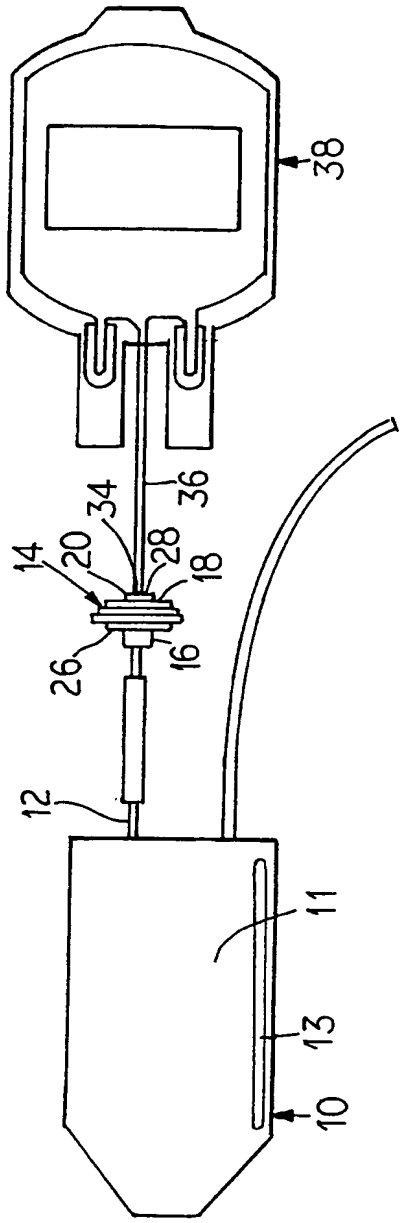
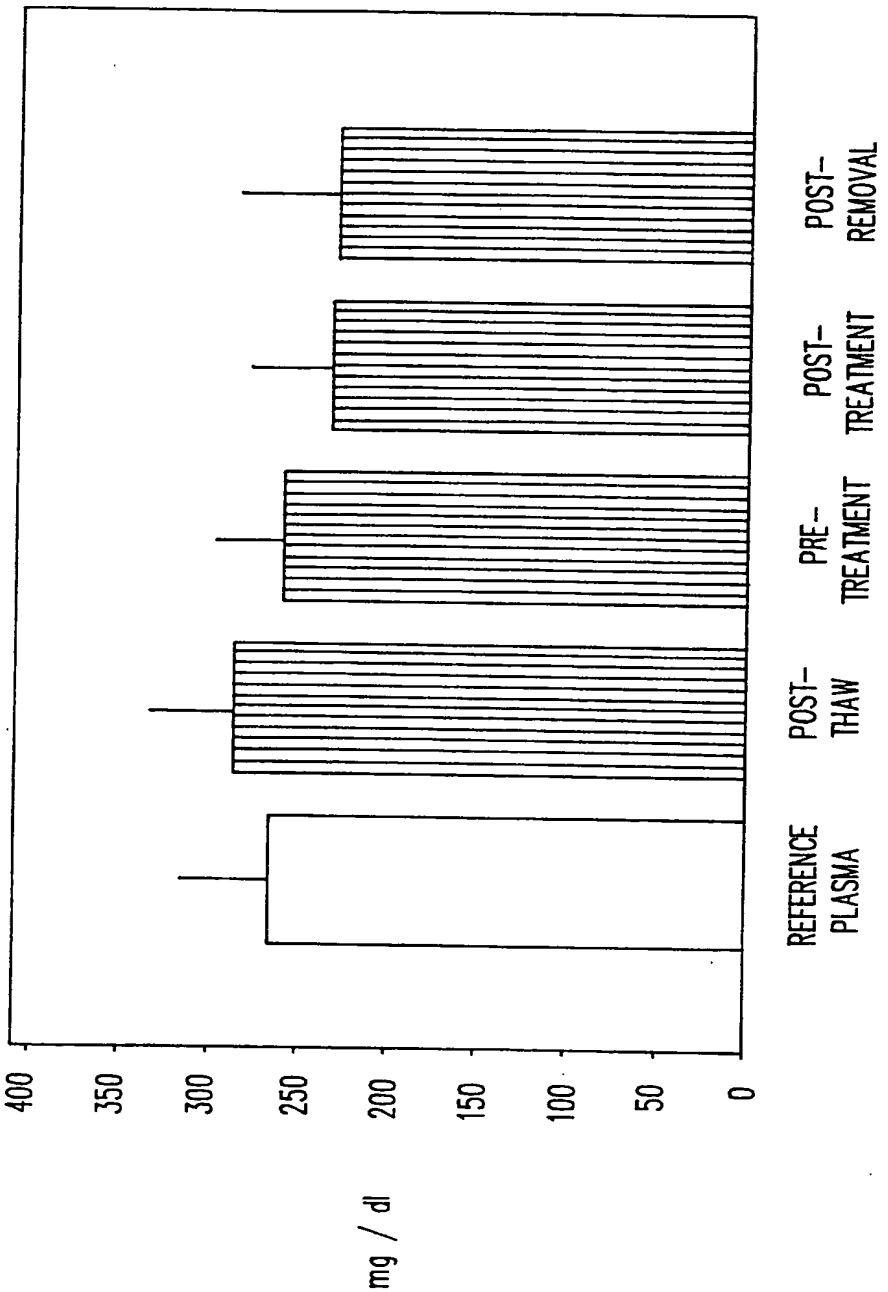


FIG. 2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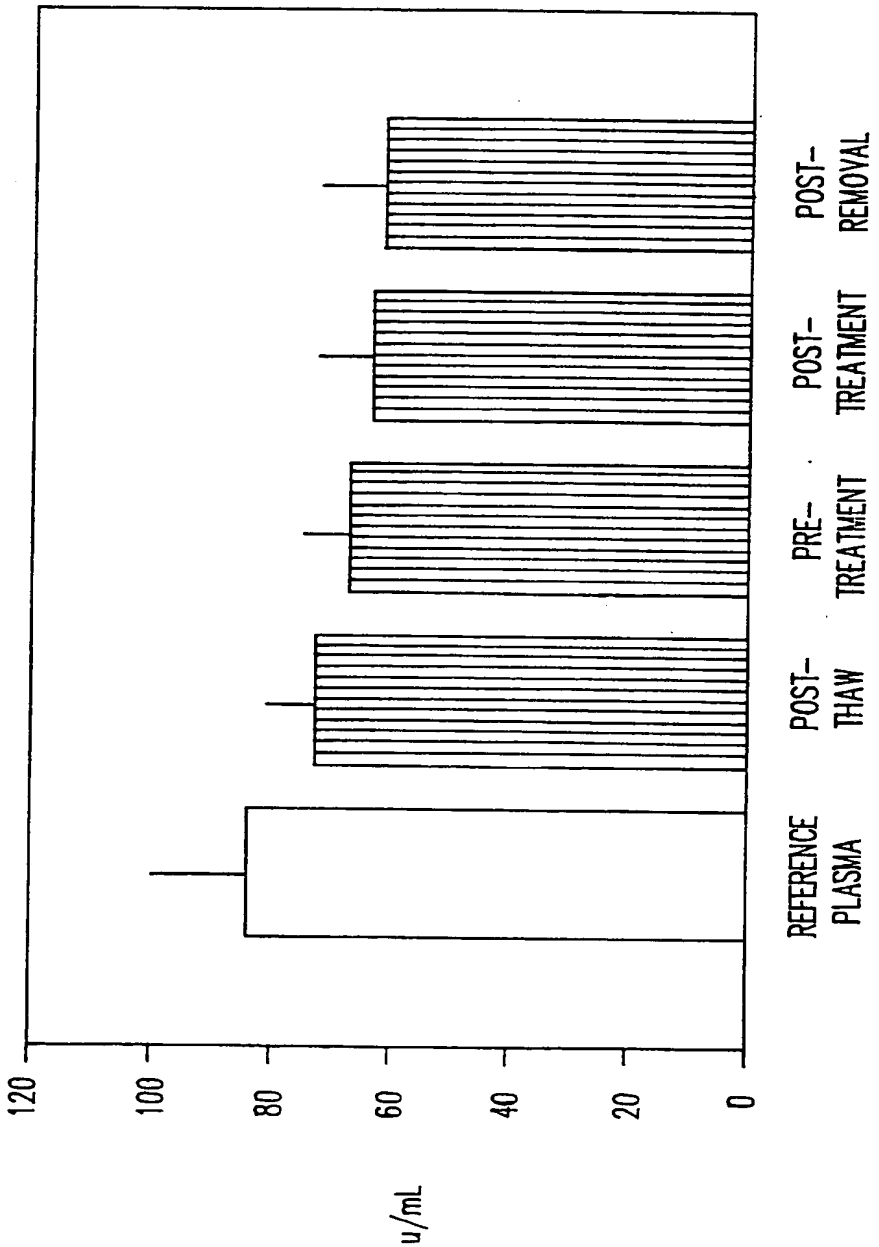
mg / dl
REFERENCE PLASMA
POST-THAW
PRE-TREATMENT
POST-TREATMENT
POST-REMOVAL

FIG. 3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REFERENCE PLASMA
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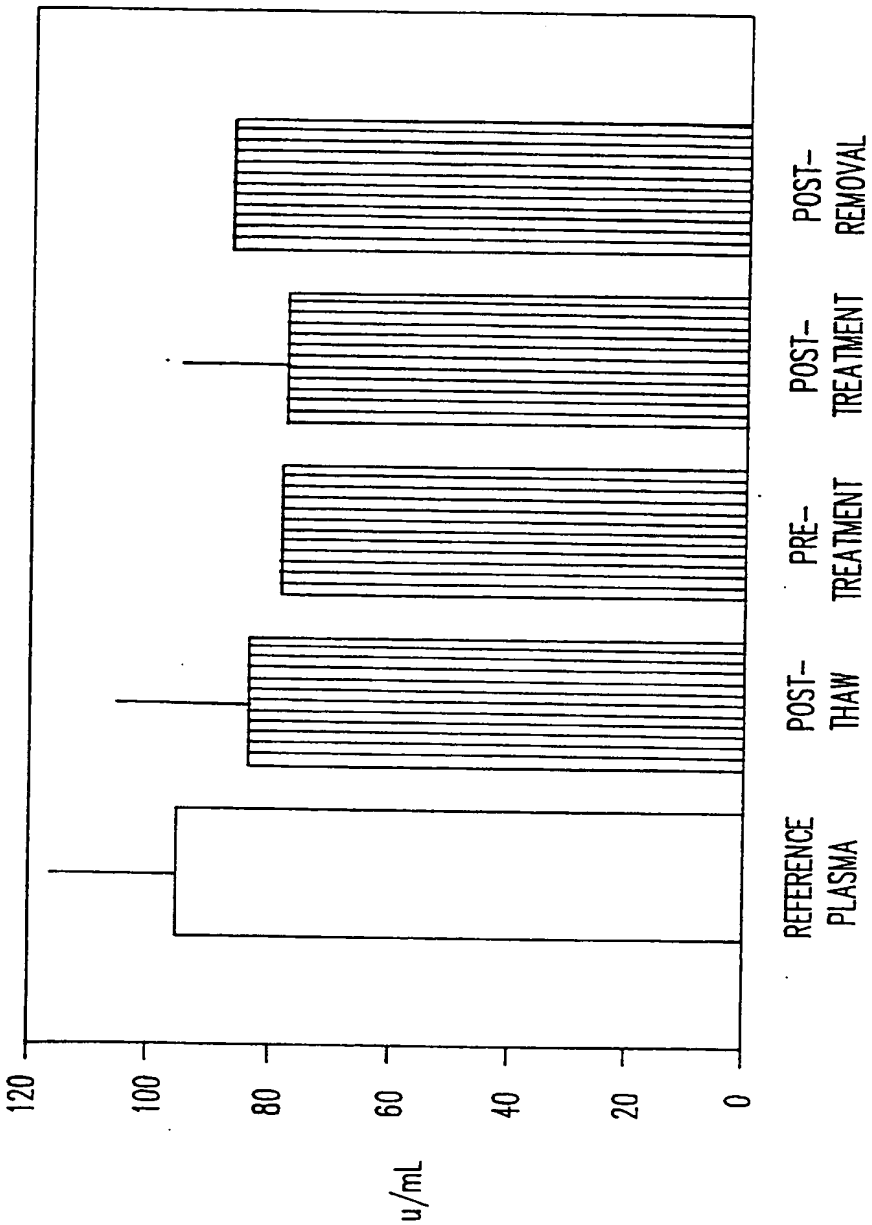
PRE-TREATMENT
POST-TREATMENT
POST-REMOVAL

FIG. 4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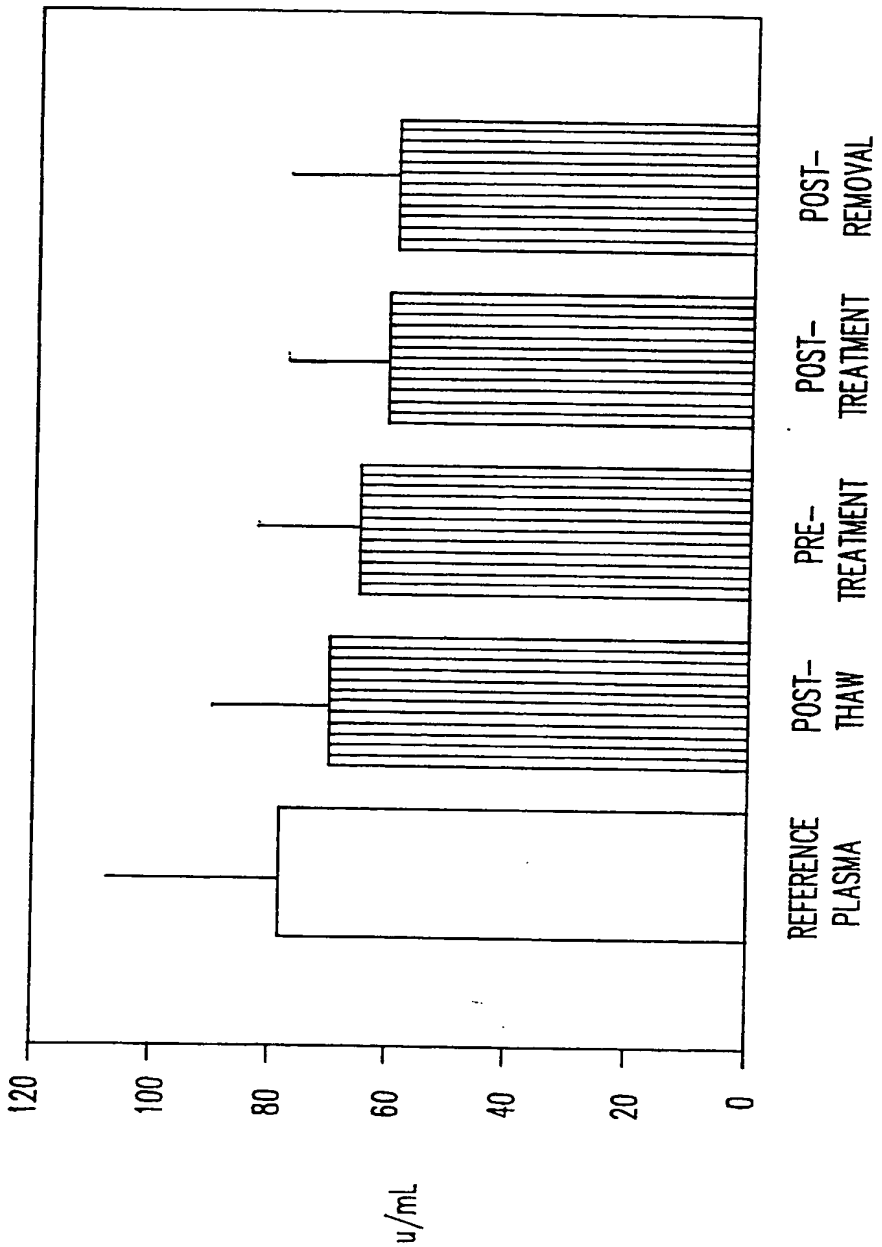
POST-THAW
PRE-TREATMENT
POST-TREATMENT
POST-REMOVAL

FIG. 5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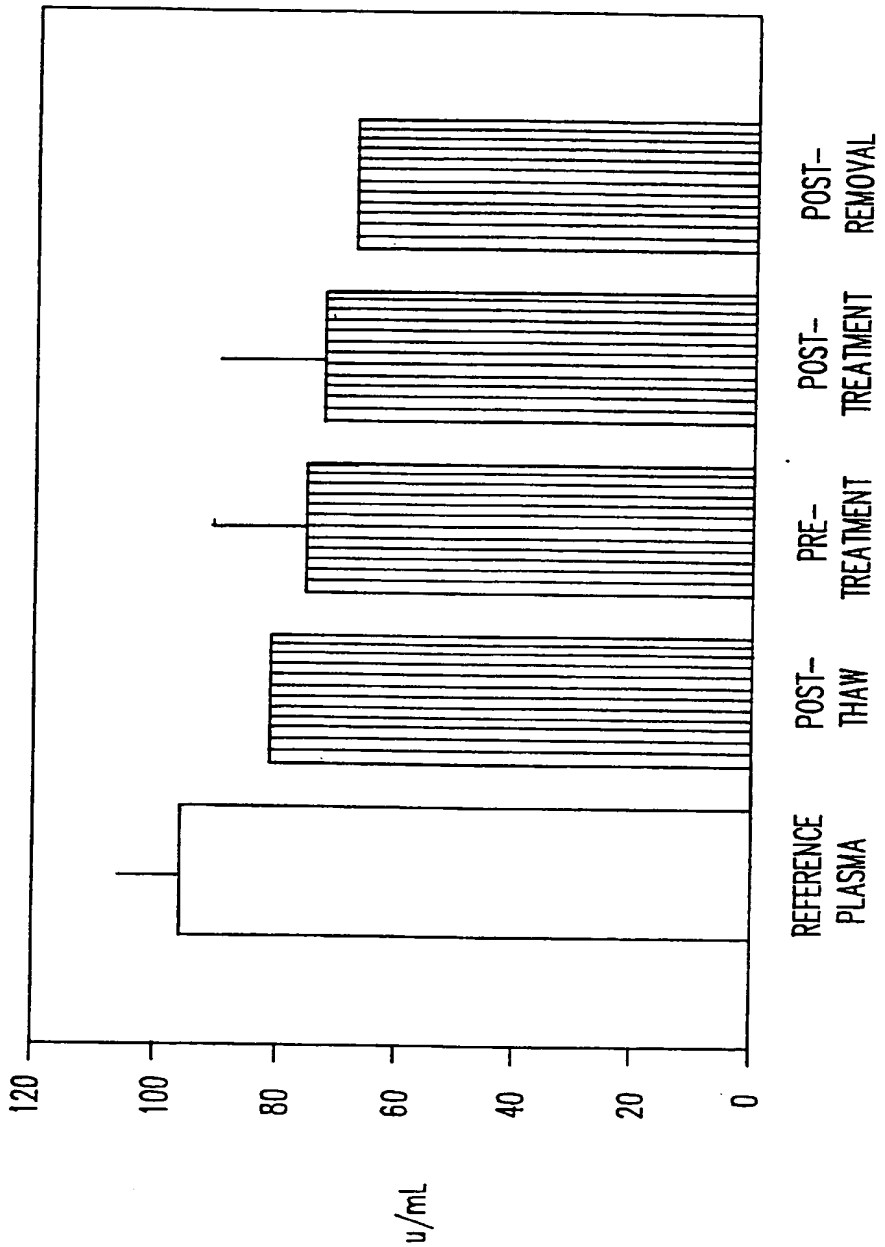
POST-TREATMENT
POST-REMOVAL

FIG. 6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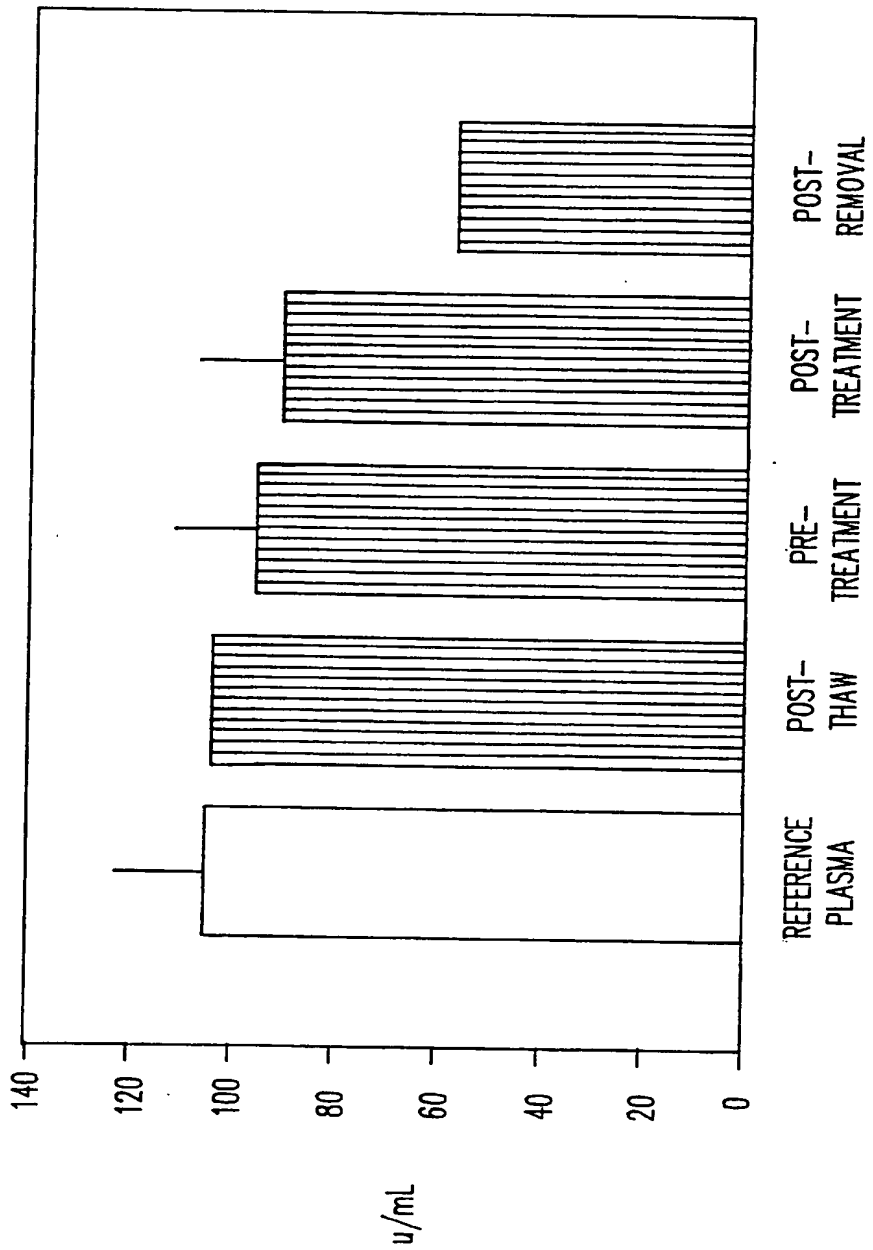
REFERENCE PLASMA
POST-THAW
PRE-TREATMENT
POST-TREATMENT
POST-REMOVAL

FIG. 7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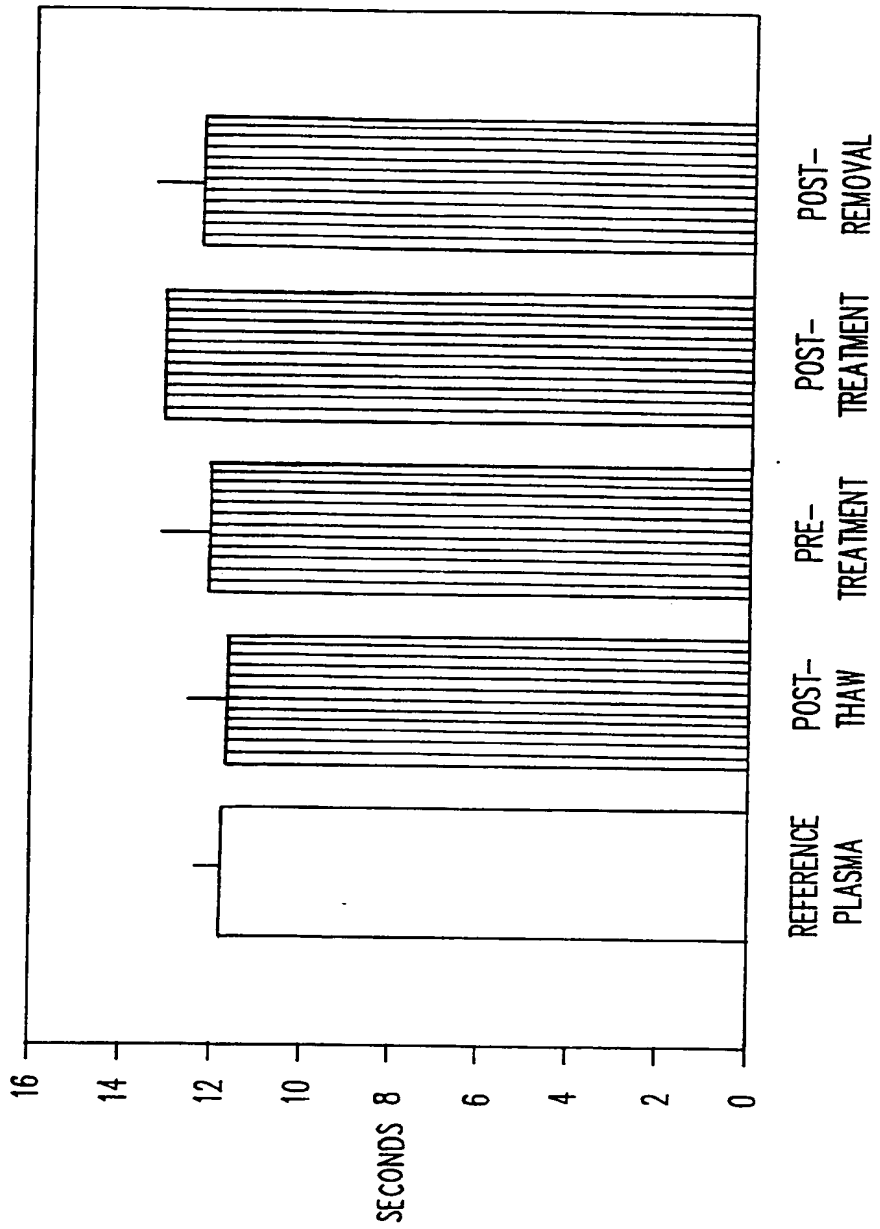
POST-TREATMENT
POST-REMOVAL

FIG. 8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POST-THAW
PRE-TREATMENT
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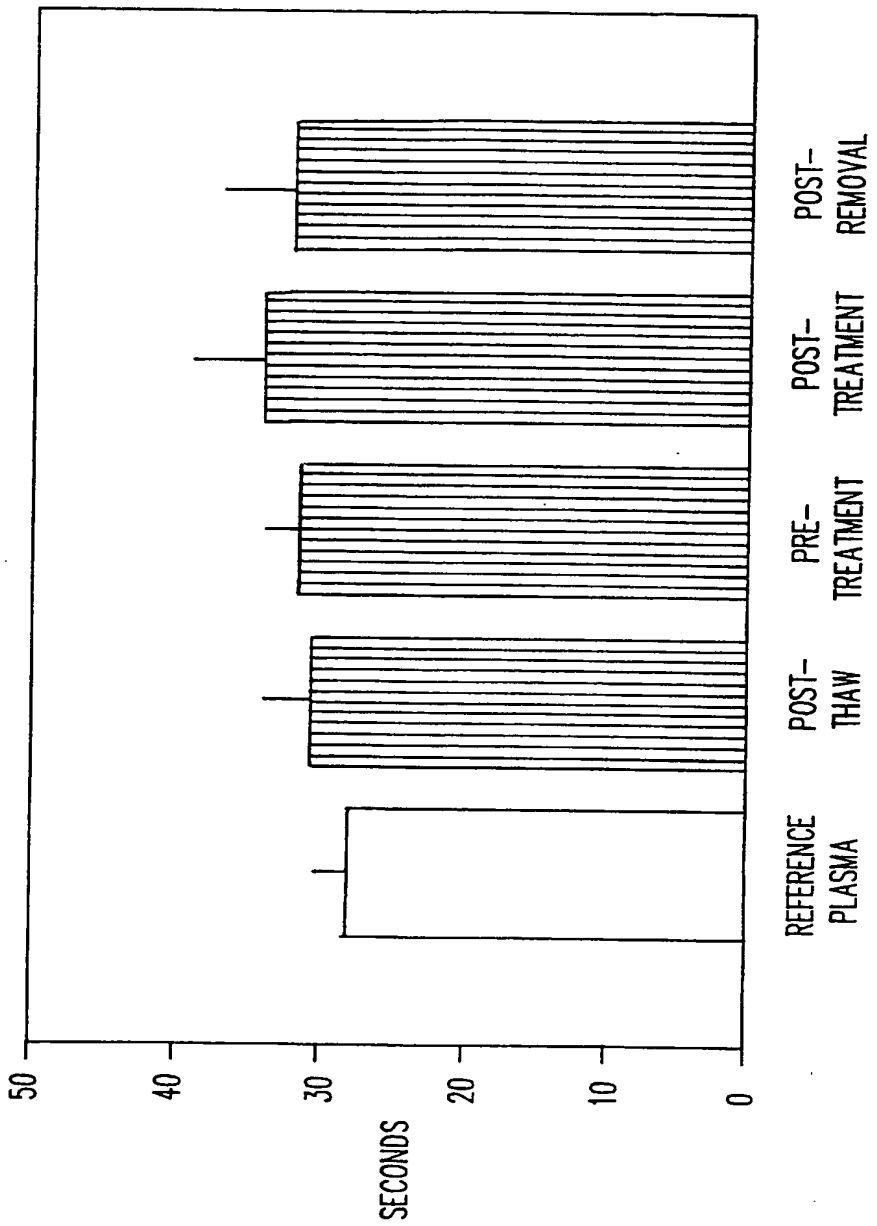
POST-REMOVAL

FIG. 9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SECONDS
REFERENCE PLASMA
POST-THAW
PRE-TREATMENT
POST-TREATMENT
POST-REMOVAL

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/14227

A. CLASSIFICATION OF SUBJECT MATTER

IPC(6) :A01N 1/02; A61K 39/12; A61M 37/00,.5/14; B01D 15/04, 15/08, 61/00
US CL :Please See Extra Sheet.
According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 210/645, 650, 651, 654, 656, 660, 679, 692; 424/89, 90, 529; 435/2; 604/4, 5, 6, 252

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

APS, Chem Abstracts, Medline, Biosis, Derwent

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	US, A, 4,878,891 (JUDY ET AL.) 07 NOVEMBER 1989, see abstract.	1-3, 5-8, 10-12, 14-23, 25-30
Y	Journal of Clinical Microbiology, Volume 17, Number 2, issued February 1983, J. Badylak et al., "Photodynamic Inactivation of Pseudorabies Virus with Methylene Blue Dye, Light, and Electricity," pages 374-376, see page 376.	1-3, 5-8, 10-12, 14-23, 25-30
Y	US, A, 4,728,432 (SUGIYAMA ET AL.) 01 MARCH 1988, see claims.	1-3, 5-8, 10-12, 14-23, 25-30
Y	US, A, 4,190,542 (HODGSON ET AL.) 26 FEBRUARY 1980, see column 2.	1-3, 5-8, 10-12, 14-23, 25-30

[X] Further documents are listed in the continuation of Box C. [ ] See patent family annex.

*	Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search 20 JANUARY 1995	Date of mailing of the international search report 13 FEB 1995
Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231 Facsimile No. (703) 305-3230	Authorized officer Ralph Gitomer Telephone No. (703) 308-0196

Form PCT/ISA/210 (second sheet)(July 1992)*

INTERNATIONAL SEARCH REPORT

International application No.
PCT/US94/14227

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	Life Science Research Products Catalog, issued 1993 by Biorad, pages 11-12.	4, 9, 13, 24
A,P	US, A, 5,294,699 (OHMURA ET AL.) 15 MARCH 1994, see entire document.	1-30
A	US, A, 3,765,536 (ROSENBERG) 16 OCTOBER 1973, see entire document.	1-30
A	Buletini I Shkencave Mjekesore, Volume 1, issued 1981, Vladimir Gusmari, "The Fractionation and Desalting of Serum Proteins and the Purification of Fluorescent Conjugates by Gel Filtration," pages 75-80, see entire translation.	1-30

INTERNATIONAL SEARCH REPORT

International Application No.
PCT/US94/14227

A. CLASSIFICATION OF SUBJECT MATTER:
US CL :

210/645, 650, 651, 654, 656, 660, 679, 692; 424/89, 90, 529; 435/2; 604/4, 5, 6, 252